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| 09/748,131      | 12/27/2000  | Yoko Aida            | P20428.P06          | 3315             |

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| EXAMINER |
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MYERS, CARLA J

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| ART UNIT | PAPER NUMBER |
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1655

DATE MAILED: 11/30/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/748,131

Applicant(s)

AIDA ET AL.

Examiner

Carla Myers

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 01 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 8, 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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1. The specification is objected to because the assigned SEQ ID NOS have not been used to identify each sequence listed, as required under 37 CFR §1.821(d). See for example, pages 8 and 9 of the specification.
2. Claims 1-4, 7-10, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to primer sets and methods of detecting nucleic acids using said primer sets wherein the primer sets are defined in terms of including a reverse primer capable of amplifying all alleles of BoLA-DRB3.2 and the forward primer is capable of amplifying all alleles in any one of two or more groups of BoLA-DRB3.2 alleles. The specification teaches a set of primers consisting of SEQ ID NO: 1-8 which hybridize to a single region within exon 2 of the BoLA-DRB3 gene and which amplify unique alleles of this gene. Accordingly, the specification has disclosed a single region of the BoLA-DRB3 gene which can be used to obtain allele and group specific primers and has adequately described forward primers consisting of SEQ ID NO: 1-8. The specification further teaches primers consisting of SEQ ID NO: 9 and 12 which amplify all alleles of BoLA-DRB3.2. However, the specification has not adequately described the broadly claimed genus of probes which are defined only in terms of their functional activity and are not defined with respect to their structural properties. It is noted that the claimed primers may be complementary to sequences in any other BoLA region because the primers only

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need to meet the limitation of being capable of amplifying all BoLA-DRB3.2 alleles or less than all BoLA-DRB3.2 alleles. It is further noted that the recitation in claims 2 and 8 that the primer comprises a portion of the DNA sequence encoding the first hypervariable region is not considered to further limit the claim because the claim does not set forth a length limitation for the "portion" and thereby the primer need only contain any, e.g., 3 nucleotides that encode any amino acid in the first hypervariable region. The specification teaches a single polymorphic region in BoLA-DRB3.2 which is useful for generating allele and group specific primers and 2 regions which can be used to generate primers which amplify all BoLA-DRB3.2 alleles. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA... requires a precise definition,

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such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of specifics have been described by their complete structure. In the instant case, only 8 members of the broadly claimed genus of forward primers and 2 members of the broadly claimed genus of primers that amplify all BoLA-DRB3.2. alleles have been defined by their structure. It is then determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In the instant case, no such identifying characteristics have been provided for any of the claimed primers. While at the time of filing applicants were in possession of primers consisting of SEQ ID NO: 1-9 and 12, the limited information provided in the specification is not deemed sufficient to reasonably convey to one of skill in the art that Applicants were in possession of a representative number of the claimed BoLA primers and thus the written description requirement has not been satisfied for the claims as they are broadly written. Applicants attention is drawn to the Guidelines for the Examination of Patent Applications under 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

3. Claims 4, 5, 10, 11, 14 and 15 objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claim not been further treated on the merits.

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4. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-15 are indefinite over the recitation of "capable of amplifying" and "incapable of amplifying" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited probes have the potential to amplify or do in fact amplify DB3.2 alleles. Amendment of the claim to read e.g. "...primer set which amplifies" would obviate this rejection.

Claims 2-6, 14 and 15 are indefinite over the recitation of "a forward primer" because it is not clear as to whether this refers to the forward primer of claim 1 or to a different primer. This rejection may be overcome by amending the claim to recite "said forward primer" or "the forward primer".

Claims 3-6, 9-11, 14 and 15 are indefinite over the recitation of "alleles of BoLA-DRB3.2 are classified into the two or more groups of alleles" and "are classified into 8 groups" because it is not clear as to how these phrases are intended to further limit the claims. The claims are drawn to a product (i.e., primer set), yet include an active process step of classifying the alleles. It is unclear as to how the step of classifying the alleles further defines the claimed primer set. The claims should be amended to clarify that the 2 or more groups comprise 96 distinct BoLA-DRB3.2 alleles.

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Claims 5, 6, and 11-15 are indefinite over the recitations of "a nucleotide sequence selected from the group consisting of the nucleotide sequences **described in...**" and "a nucleotide sequence described in" because it is not clear as to whether the claims are limited to primers which comprise the full length sequence of the stated SEQ ID NO or which comprise only a portion (1 or 2 nucleotides, etc.) of the stated SEQ ID NO. This rejection may be overcome by amendment of the claims to recite "wherein said primer comprises any one of the sequences of SEQ ID NO: 1-8".

Claims 14 and 15 are indefinite for failing to recite a final process step which agrees back with the preamble. The claims are drawn to methods for typing polymorphisms, yet recite the final step of comparing the resulting sequences with known alleles. The claims should be amended to clarify how comparing the step of comparing the sequences with known alleles results in the typing of polymorphisms.

Claims 14 and 15 are further indefinite over the recitation of "resulting sequences". It is unclear as to what constitutes resulting sequences because claims do not recite a step of generating resulting sequences.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

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has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-4, 7-10 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Ellegren et al (Animal Genetics (1993) 24: 269-275).

Ellegren et al teaches allele-specific primers which hybridize to unique sequences in the BoLA-DRB3.2 gene (page 270). These oligonucleotide primers are considered to be capable of amplifying all alleles in one of two or more groups since the 5 oligonucleotides amplify distinct BoLA-DRB3.2 alleles. It is noted that the claims and specification do not define particular groups, and thereby the alleles may be divided by any criteria into groups. Thus, the oligonucleotide primers are each considered to be capable of amplifying alleles of one group and not alleles of any of the remaining 7 groups. The oligonucleotides are also considered to comprise a portion of a DNA sequence encoding an amino acid sequence of the first hypervariable region of BoLA-DRB3.2 since the oligonucleotides comprise at least one nucleotide of the same identity as a nucleotide in the stated DNA sequence. Furthermore, Ellegren teaches performing PCR using one of the allele-specific primers together with the LA31 primer. In the absence of evidence to the contrary, the general LA31 primer is considered to be a primer which is capable of amplifying all BoLA-DRB3.2 alleles. With respect to claim 14, Ellegren further teaches sequencing the amplified DRB3.2 alleles (see page 272).

6. Claims 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Sitte (Animal Genetics (1996) 27: 271-273).



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Sitte (page 272) teaches an oligonucleotide which hybridizes to all but one BoLA-DRB3.2 alleles. The oligonucleotide is considered to have the properties of a primer since it may be extended at the 3' end. Furthermore, the oligonucleotide is considered to be capable of amplifying all alleles in one of two or more groups since the oligonucleotide would be useful for amplifying all non-BoLA-DRB3.2\*A alleles (group 1) and does not amplify BoLA-DRB3.2\*A alleles (group 2). The oligonucleotide is also considered to comprise a portion of a DNA sequence encoding an amino acid sequence of the first hypervariable region of BoLA-DRB3.2 since the oligonucleotide comprises at least one nucleotide of the same identity as a nucleotide in the stated DNA sequence.

7. Claims 1-4, 6-10 are rejected under 35 U.S.C. 102() as being anticipated by Aida (US Patent No. 6,284,457).

Aida (column 7) teaches a primer B which is identical to instant SEQ ID NO: 9 and thereby has the property of being capable of amplifying all alleles of BoLA-DRB3.2. Aida (column 7) also teaches a primer A which hybridizes to the same polymorphic region to which the instantly claimed primers of SEQ ID NO: 1-8 hybridize. Primer A is considered to have the property of being capable of amplifying all alleles in one of two or more groups or 8 groups since the primer would be useful for amplifying only alleles that are fully complementary to the primer or share high levels of sequence complementarity to the primer under high stringency conditions and the primer is considered to be incapable of amplifying alleles that do not share high levels of sequence complementarity. Again, it is noted that the claims and specification do

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not define the alleles which constitute each group. The primer is also considered to comprise a portion of a DNA sequence encoding an amino acid sequence of the first hypervariable region of BoLA-DRB3.2. With respect to claim 14, Aida further teaches sequencing the amplified DRB3.2 alleles (see column 8).

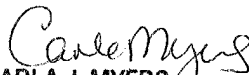
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is (703) 308-2199. The examiner can normally be reached on Monday-Thursday from 6:30 AM-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703)-308-1152. The fax number for the Technology Center is (703)-305-3014 or (703)-305-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

Carla Myers

November 27, 2001

  
CARLA J. MYERS  
PRIMARY EXAMINER